FACT SHEET 1

INTRODUCTION TO BIOLOGICS

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INTRODUCTION TO BIOLOGICS

Biologics are medicinal products whose active substance is made by a living organism.

A biologic medicine (also known as a biologic) is any medicine made using a living organism. They are increasingly important in the treatment of serious, debilitating, and life-threatening diseases including cancers, rheumatoid arthritis, and rare diseases. Biologics are different from traditional chemically synthesized drugs. They are larger and more complex molecules and because they are made from living organisms, they are inherently more variable.

This appendix addresses key differences between biologics from conventional chemically synthesized drugs and discuss implications for their manufacturing, development and delivery to patients.

BIOLOGICS: THE NEXT GENERATION OF THERAPEUTIC INNOVATION

Any medicinal product originated from a living organism can be considered to be a **biologic product**. This includes blood and plasma derived-products, but also **biologically engineered proteins** produced by bacteria or other living system. For the purpose of this review we will focus on the latter, and we will be using the term **"Biologic medicine"** or **"Biologic"** to refer to **"all biologically active protein products which are used in the treatment of human diseases."** [1] This is The World Health Organization's definition for **biotherapeutic protein products prepared by recombinant DNA technology, which comprise most of the biologics used today, and will be the focus of this review.**

Biologics have been in existence for several decades. However, modern biotechnology techniques introduced in recent years have greatly enhanced the ability to develop biologics safely and consistently (Figure 1). Biologics are currently available to treat many life-threatening and life-altering diseases such as cancer, rheumatoid arthritis, and multiple sclerosis, and many rare diseases for which there were no previous treatment options. The global market share of biologics is anticipated to rise from 11% in 2002 to 20% by 2017.[2]

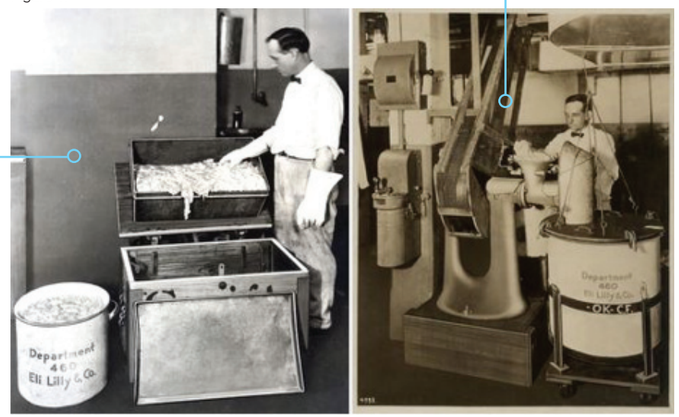
EVOLUTION IN DEVELOPMENT OF BIOLOGICS

THEN

Insulin was one of the first biologic medicines. Manufacturing processes that pre-dated biologic processes were expensive and wasteful. Almost two tonnes of pig pancreas were required to extract just a small vial of insulin.[3]

The glands are run through grinders prior to insulin extraction.

Figure 1.



Pig pancreas glands from meatpacking factories under examination upon arrival.

Source: The National Museum of American History (2013) [3]

SOURCES

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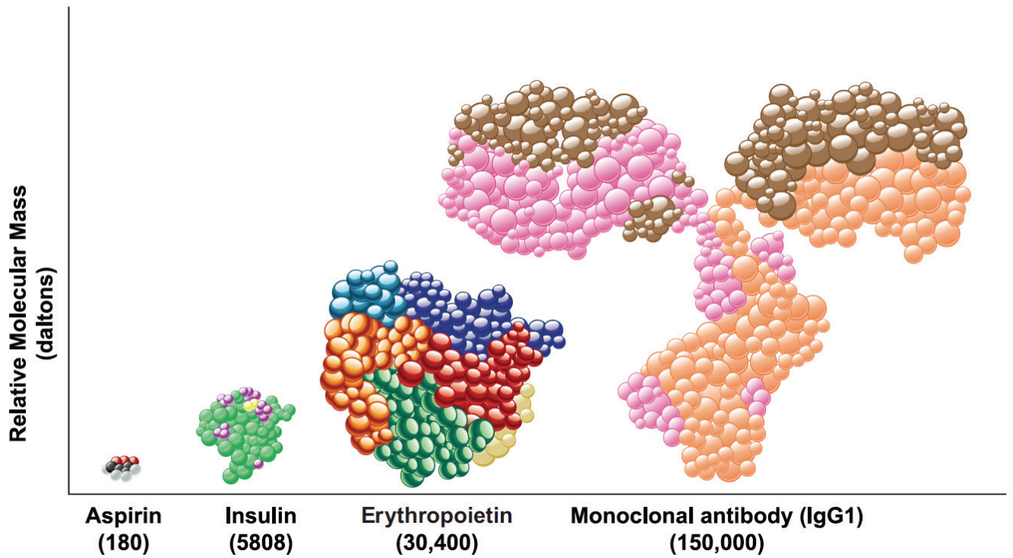
COMPARING THE SIZE & STRUCTURE OF BIOLOGICAL MEDICINES TO SMALL-MOLECULE MEDICINES

Figure 3.



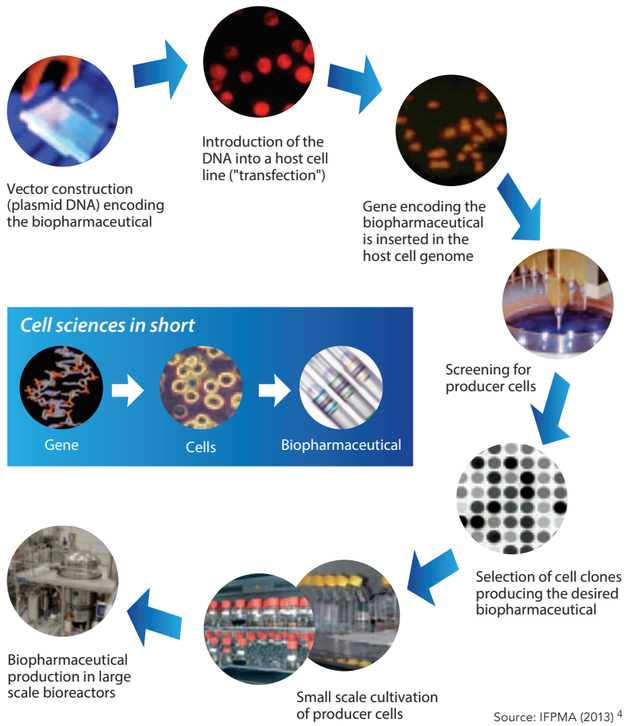
Source: Mellstedt H. Clinical considerations for biosimilar antibodies (2013) [8]

NOW

Today, recombinant DNA technology allows us to genetically re-programme cells to produce insulin safely and efficiently, within highly-controlled conditions, giving patients wider access to insulin with consistent quality, safety, and efficacy without animal contaminants.

THE PROCESS OF PRODUCING BIOLOGICS TODAY

Figure 2.



Source: IFPMA (2013) [4]

HOW ARE BIOLOGICS DIFFERENT FROM CHEMICALLY SYNTHESIZED DRUGS?

Biologics are different from conventional small-molecule medicines, which are typically made from chemical synthesis.

Biologics differ from conventional medicines in several ways[6]:

Synthesis

Biologics are made using living organisms (**Figure 2**) whereas small-molecule medicines are made by chemical synthesis

Size and structure

Biologics are large and complex protein molecular structures, whereas chemically synthesized drugs are typically small molecules (**Figure 3**).

Manufacturing

Biologics are made from living organisms, and the final product depends on the genetic sequence that was cloned but also the manufacturing process, in which slight variations may be introduced. In contrast, all copies of a small molecule drug are identical.

Characterisation

Due in part to their large size and complexity, it may be difficult to anticipate the effect of a biologic in any specific individual. In contrast, it is relatively easy to use analytical methods to define the active pharmaceutical ingredient and thereby predict the clinical effect of a chemically synthesized drug.

Stability

Compared to small molecule medicines, biologics are much more sensitive to handling and storage conditions during manufacturing and distribution because they are made from living organisms and are larger in size.

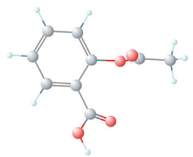
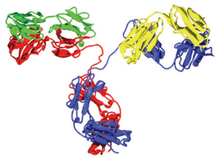
Immunogenicity

Compared to small molecule medicines, biologics are more likely to cause an immune response because of their complex structure and unique product characteristics due to their biological nature.

These differences are summarised in Table 1.

THE DIFFERENCES BETWEEN SMALL-MOLECULE MEDICINES & BIOLOGICAL MEDICINES

Table 1.

	Small-Molecule Medicines (chemical-based)	Biological Medicines (protein-based)
Example	 Acetylsalicylic acid (anti-inflammatory & pain relief) [5]	 Monoclonal antibody (treats cancer & autoimmune diseases) [6]
Molecular Weight	180 daltons [9]	~144,000 daltons [10]
Size	Small [11]	Large [11]
Structure	Simple and well defined [11]	Complex [12]
Manufacturing	Predictable chemical process; Identical copies can be made.[12]	Each manufactured in a unique living cell line; similar-but-not-identical copies can be made.[12]
Characterisation	Easy to fully characterise [12]	Difficult to fully characterise [12]
Stability	Usually stable [12]	More sensitive than small-molecule medicines to handling and storage conditions [12]
Immunogenicity	Usually unexpected [11]	Higher potential; always need to be tested during development [11]

Source: Carton JM & Strohl WR. Protein therapeutics) [7]